Translation

PCT/FR2003/003205

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference BCT030126 | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| International application No. PCT/FR2003/003205 | International filing date (*day/month/year*) 28 octobre 2003 (28.10.2003) | Priority date (*day/month/year*) 29 octobre 2002 (29.10.2002) |
| International Patent Classification (IPC) or national classification and IPC C07D 493/10 | | |
| Applicant LABORATOIRES SYNTH-INNOVE | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 10 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 28 avril 2004 (28.04.2004) | 10 February 2005 (10.02.2005) |
| Name and mailing address of the IPEA/EP<br><br>Facsimile No. | Authorized officer<br><br>Telephone No. |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR2003/003205

## I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed

☒ the description:

pages 1,2,4-7,9-24, as originally filed
pages _____, filed with the demand
pages 3,8, filed with the letter of 27 May 2004 (27.05.2004)

☒ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages 1-22, filed with the letter of 27 May 2004 (27.05.2004)

☒ the drawings:

pages 1-6, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 3-14 | YES |
| | Claims | 1, 2, 15-22 | NO |
| Inventive step (IS) | Claims | 3-14 | YES |
| | Claims | 1, 2, 15-22 | NO |
| Industrial applicability (IA) | Claims | 1-22 | YES |
| | Claims | | NO |

2. Citations and explanations

Reference is made to the following documents:

D1: US-A-5 637 733 (SUJEETH PUTHALATH K)
10 June 1997 (1997-06-10)

D2: DE 360 691 C (MONSANTO CHEMICAL WORKS)
6 October 1922 (1922-10-06)

D3: SHAWN C. BURDETTE ET AL.: "Fluorescent sensors for Zn2+ based on a fluorescein platform: Synthesis, properties and intracellular distribution" J. AM. CHEM. SOC, vol. 123, 2001, pages 7831-41, XP002248841

**1. Corrections (PCT Article 28(2) and PCT Rule 91)**

The corrections in claims 1 and 3 and the corresponding parts of the description are obvious (PCT Rule 91) and do not contravene PCT Article 28(2).

The correction in the new claim 12, which corresponds to the original claim 11, is acceptable since "crystal of red" clearly means "crystal of red colour".

Claims 8 to 11 are acceptable as concerns PCT Article 28(2).

**2. Novelty (PCT Article 33(1))**

The present application does not meet the requirements of PCT Article 33(1) as the subject matter of claims 1, 2 and 15 to 22 does not meet the novelty requirement of PCT Article 33(2).

D1 describes a method of producing fluorescein (examples 1 and 2) by condensing resorcinol with phthalic anhydride and without solvent. This teaching destroys the novelty of claims 1 and 2. The fact that the phthaleins in the present application are purer than the prior art compounds does not render the subject matter of the present application novel. Hence claims 15, 18, 19 and 22 are not novel either. D5 describes a method of purifying fluorescein. The resultant fluorescein can be used in pharmacy. This teaching proves that fluorescein can be purified and that a purified fluorescein is not novel. For a method to render a compound novel, all the prior art methods have to be incapable of purifying fluorescein (T 990/96). It appears possible to obtain a fluorescein by purification methods (e.g. D1). Therefore, the claims concerning purified fluorescein are not novel within the meaning of PCT Article 33(2).

In D1, example 3, 3,4,5,6-tetrachlorofluorescein is produced. The subject matter of example 3 destroys the novelty of claims 1, 2, 18 and 22.

D2 describes the production of phenolphthalein by condensation of phthalic anhydride with phenol and without solvent (example 1). In example 3, gallein (4',5'-dihydroxyfluorescein) is produced by the condensation of phthalic anhydride with pyrogallol, also without the use of a solvent. This teaching destroys the novelty of claims 1, 15, 17, 18, 21 and 22.

D3 describes the production of 4',5'-dimethylfluorescein (Experimental Section, production of compound 1). This subject matter destroys the novelty of claims 1, 16, 18, 20 and 22.

**3. Clarity (PCT Article 6)**

The application does not meet the requirements of PCT Article 6 since claims 15 to 17 are unclear.

The compounds in claims 15 to 17 are characterized by their colours and radio-crystallography spectra. These compounds are produced by the reaction of a red phthalein with an acid in an anhydrous solvent selected from the group comprising alcohols, ketones, ethers, halogenated solvents or mixtures thereof. In light of the description, it is not clear what happens to the phthaleins in the above-mentioned method. An acid addition salt of the phthalein compound may be formed after the reaction with an acid.